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Closing-in Behavior in Mild Cognitive Impairment: An Executive Deficit

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Abstract

This study explored Closing-in behavior (CIB), the tendency in figure copying to draw very close to or on top of the model, in mild cognitive impairment (MCI). The files of 154 people diagnosed with MCI were reviewed and CIB was identified in 21% of cases. Two approaches were used to explore CIB. First, we capitalized on the diverse cognitive profiles within MCI, subdividing the overall sample into people with and without memory deficits. The frequency of CIB was significantly higher in multidomain non-amnesic MCI than in multidomain amnesic MCI, suggesting that CIB is not associated with specific memory impairment. Second, we assessed the cognitive correlates of CIB, by selecting patients with MCI who completed a battery of executive, visuo-constructional and memory tasks. Sub-groups of patients with and without CIB showed a similar overall severity of cognitive decline and comparable performance in visuo-constructional and memory tasks, but those with CIB were slightly but significantly more impaired on executive function tasks. The study provides evidence against memory-based accounts of CIB, and supports recent suggestions that executive impairments are the dominant cognitive correlate of this clinical sign. (*JINS*, 2012, *18*, 269–276)

Keywords: Closing-in behavior, Constructional abilities, Executive control, memory, Visuo-spatial abilities, Mild cognitive impairment

INTRODUCTION

In clinical assessments of copying, the copy may sometimes be made inappropriately close to the model, a behavior known as “closing-in behavior” (CIB) (Mayer Gross, 1935; McIntosh, Ambron, & Della Sala, 2008). This sign can take different forms, varying in severity from veering toward the model (“near type” CIB) to drawing directly over it (“overlap type CIB”). CIB has been often associated with poor fidelity of the copy (Gainotti, 1972), consistent with its classical interpretation as an aspect of constructional apraxia (Critchley, 1953).

CIB has been noted in a variety of brain diseases, including stroke, carbon monoxide poisoning, corticobasal degeneration, encephalitis, and epilepsy (Conson, Salzano, Manzo, Grossi, & Trojano, 2009; De Ajuriaguerra, Zazzo, & Granjon, 1949; Kwon et al., 2002; Muncie, 1938; Stengel & Vienna, 1944;

Suzuki et al., 2003). However, it is most frequent in patients with dementia and becomes more common with increasing dementia severity (Gainotti, 1972). In particular, CIB has been considered as a typical manifestation of Alzheimer’s disease (AD) (Gainotti, Marra, Villa, Parlato, & Chiarotti, 1998), although recent evidence suggests that the phenomenon may be equally common in other forms of dementia, such as vascular dementia (Chin et al., 2005) or fronto-temporal dementia (Ambron, Allaria, McIntosh, & Della Sala, 2009).

The cognitive nature of CIB has been debated recently (Ambron, McIntosh, Allaria, & Della Sala, 2009; Serra, Fadda, Perri, Caltagirone, & Carlesimo, 2010), and two main hypotheses have been put forward to account for it: the “compensation hypothesis” and the “attraction hypothesis.” Neither hypothesis excludes some involvement of visuo-spatial deficits, but they differ over the main cognitive deficit responsible for CIB. The compensation hypothesis implicates memory impairments as the major causes of CIB, and posits that the copy is made in close proximity to the model to compensate for an inability to remember its representation for long enough to

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transpose it to a remote location (Lee et al., 2004). The attraction hypothesis instead considers CIB to reflect the disinhibition of an automatic tendency to act towards the focus of attention. Advocates of this latter hypothesis suggest that attention and executive deficits are the main factors responsible for the release of CIB (Kwon et al., 2002; McIntosh et al., 2008).

Although CIB has been strongly linked with dementia, it is not known whether it can be observed in mild cognitive impairment (MCI) (Petersen et al., 1999, 2001), a “transitional zone between normal cognitive function and dementia” (Kume et al., 2011). However, if CIB does arise in MCI, this would offer a valuable opportunity to test whether or not memory impairment plays a significant role in this sign (Lee et al., 2004). People with MCI can present with memory problems, either in isolation or in conjunction with other cognitive impairments, whereas others have deficits in other cognitive domains (attention, executive functions, language, visuo-spatial abilities), without memory problems (Winblad et al., 2004). If memory is critical, then CIB should differentially affect people with amnesic forms of MCI.

To address this question, we have reviewed the clinical records of a sizeable sample of people with MCI ($n = 154$). Beyond the primary distinction between amnesic and non-amnesic sub-groups, we were also able to identify a sub-sample of 86 people with MCI who had completed the same test battery assessing executive, visuo-spatial and memory tasks, allowing for further exploration of the cognitive determinants of CIB in MCI.

METHODS

Participants and Cognitive Assessment

This retrospective study explored CIB in MCI using two approaches. First, a total of 313 neuropsychological records of MCI patients were reviewed. These patients attended the Neurology Ward, Sacco Hospital, Milan, Italy, from 2001 to 2010. Records were included that met the following criteria: (1) clinical diagnosis of MCI (Winbland et al., 2004); (2) Mini Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975) score equal to or above 26; and (3) availability of original response sheet for the Rey Figure Copying Task (Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2002a; Osterrieth, 1944; Rey, 1941). There were 154 patients fulfilling these criteria (78 males and 76 females). Their median age was 75.3 years (range, 46–88 years), their median education was 8 years (range, 1–19 years), and their median MMSE score was 27 (range, 26–30). A variety of cognitive tasks were used to explore the cognitive profile of this cohort (see Table 1). These tasks (see Table 1) had not been determined in advance, but were selected individually by clinicians for each patient. All the tasks used for the neuropsychological assessment have published norms and cut off scores derived from Italian populations.

We classed MCI patients, according to the criteria of Winbland et al. (2004), as: (i) *single-domain amnesic*, if they showed a specific impairment in memory, performing below the cutoff in one or more of the memory tasks; (ii) *multidomain*

amnesic if they showed impairment in memory *and* in one or more other cognitive domains (intelligence, visuo-spatial and visuo-constructional abilities, language, attention, and executive functions); (iii) *single-domain non-amnesic*, if they showed a specific impairment in a single cognitive domain, performing below the cutoff in one or more tasks belonging to one non-memory domain, but normal performance on all memory tasks; (iv) *multidomain non-amnesic*, if they showed impairment in more than one cognitive domain, but normal performance on memory tasks.

A sub-group of the total MCI cohort was identified that had been assessed with an identical battery of cognitive tasks, covering memory, visuo-spatial abilities and executive functions. There were 86 patients in this sub-group (48 males and 38 females), with a median age of 76.0 years (range, 50–88 years), a median education of 8 years (range, 3–18 years), and a median MMSE score of 28 (range 26–30). These patients had all completed five tests of relevance to our research questions, described below: Raven Progressive Matrices Test (Basso, Capitani, & Laiacina, 1987; Raven, 1965), Rey Figure Drawing from Memory (Caffarra et al., 2002a), Trail Making A (Giovagnoli et al., 1996), Clock Drawing Test (Sunderland et al., 1989), and the Frontal Assessment Battery (Appollonio et al., 2004; Dubois, Slachevsky, Litvan, & Pillon, 2000).

Raven Progressive Matrices Test (Basso et al., 1987; Raven, 1965) requires completion of 2×2 matrices in which one element is missing, and is considered as an overall measurement of intelligence and logical reasoning. The *Rey Figure Drawing from Memory Task* assesses the accuracy of reproduction of the Rey Complex Figure, after a delay of approximately 15 min. This was considered as a test of memory, although with a strong visuo-spatial component. The *Trail Making A* and the *Clock Drawing Test* were taken as immediate measures of visuo-spatial abilities. Trail Making requires visual scanning and visuo-motor accuracy since participants are asked to connect a series of numbers presented in circles, as fast as they can; in the Clock Drawing task, people are asked to draw a clock and to set the time at 45 min past two. This task is used as a test of constructional abilities, but it also requires some level of executive control (Cosentino, Jefferson, Chute, Kaplan, & Libon, 2004). Finally, the total score of the *Frontal Assessment Battery* (FAB: Appollonio et al., 2004; Dubois et al., 2000) was included as an assessment of executive functions. The FAB includes six sub-tests: *Similarities*, *Lexical fluency*, *Motor series*, *Conflicting instructions*, *Go-No-Go*, and *Prehension behavior*.

All patients whose records have been included in the present study signed an informed consent for the use of their data for research purposes. Moreover, ethical approval for the study was obtained from the medical ethics committee of Luigi Sacco Hospital.

Assessment of CIB

The patients' immediate Rey figure copies were scored for CIB and for copy accuracy, using criteria identical to those previously applied to score the performance of patients with AD

Table 1. Tasks used for the cognitive assessment of people with MCI with their relative score range and cutoff scores

Tasks	Range	Cutoff
<i>Memory</i>		
Digit Span (Orsini et al., 1986)	0–9	3.75
Corsi Block Test (Spinnler & Tognoni, 1987)	2–10	3.5
Prose Memory (Spinnler & Tognoni, 1987)	0–16	4.75
Prose Memory (Novelli et al., 1986)	0–28	8
Rey Auditory Verbal Learning Test (Carlesimo et al., 1996)		
Learning phase	0–85	28.53
Recall phase	0–15	4.69
Memory for Figures (Pomati et al., 2003)		
Learning phase	0–45	20.6
Recall phase	0–15	4.69
Rey Figure – drawing from memory (Caffarra et al., 2002a)	0–36	9.47
<i>Intelligence</i>		
Raven Progressive Matrices (Basso et al., 1987)	0–36	18
Weigl Sorting Test (Laiacina et al., 2000)	0–15	8
<i>Language production</i>		
Semantic Fluency (Novelli et al., 1986)	NA	25
<i>Visuo-spatial abilities</i>		
Rey figure – copy (Caffarra et al., 2002a)	0–36	28.88
Clock Drawing Test (Sunderland et al., 1989)	0–16	6
Line Orientation (Benton et al., 1978)	0–30	17
Trail Making A (Giovagnoli et al., 1996)	0–180	93
<i>Executive functions</i>		
Rey Figure – copy procedure (Osterrieth, 1944)	1–7	3
Phonetic Verbal Fluency (Novelli et al., 1986)	NA	17
Frontal Assessment Battery (Appollonio et al., 2004)	0–18	13.5
Stroop Test (Caffarra et al., 2002b)	NA	36.91
<i>Attention</i>		
Attentional Matrices (Della Sala et al., 1992)	0–60	30

Note. All these tasks have published norms and cutoff scores. NA, not available.

(Ambron, McIntosh, et al., 2009). CIB was scored as present when the copy invaded the model's space, or touched the edges of the model (overlap type), or if it was placed in close proximity to the model (≤ 10 mm distance with the model) (near type). The use of this latter, more liberal criterion for CIB, maximizes sensitivity to mild manifestations of this sign, which might be expected among patients with MCI. The accuracy of the copy was assessed independently of its positioning, being rated as poor when the original model was not recognizable or was only partially recognizable, and as accurate if the original model was recognizable.

RESULTS

In line with previous evidence (Rasquin, Lodder, Visser, Lousberg, & Verhey 2005), we found that multidomain MCI subtypes ($n = 127$; 82%) were more common than single-domain subtypes ($n = 27$; 18%). Multidomain amnesic was the most common ($n = 98$; 63%), followed by multidomain non-amnesic MCI ($n = 29$; 19%), whereas 15 (10%) and 12 (8%) people respectively were affected by single-domain amnesic and non-amnesic subtypes. The primary cognitive

domains affected in the non-amnesic MCI groups were executive functions in the single-domain non-amnesic MCI ($n = 8$; 66%) and visuospatial abilities in the multidomain non-amnesic MCI ($n = 25$; 86%). Visuospatial deficits in this group were related in most of the cases ($n = 23$; 79%) to poor performance in the Rey Figure copying task.

Overall CIB was identified in 33 cases (21% of total sample), the clear majority being of the near-type ($n = 27$), with the overlap type observed in only 6 cases. The presence of CIB did not correlate with demographic characteristics (age: $\rho = -.048$, n.s.; education: $\rho = -.048$, n.s.) or with MMSE score ($\rho = .062$, n.s.). Of interest, CIB did not correlate significantly with copy accuracy judged from the same drawings ($\rho = .09$, n.s.), being associated with good copy accuracy only slightly less often than with poor accuracy ($n = 13$ vs. $n = 20$), and poor copy accuracy being quite often observed without CIB ($n = 51$). Regarding the copying procedure, most of the patients with CIB ($n = 24$; 73%) showed a tendency to reproduce the shape in a segmented manner, such that they appeared to be adding the different elements of the figure as if composing a puzzle ($n = 12$; 36.5%) or drawing them independently without providing a

Table 2. Median, range and Mann-Whitney *U* test results of the demographic characteristics and performance in the different cognitive tasks of MCI with and without CIB

	MCI with CIB (<i>n</i> = 17)	MCI without CIB (<i>n</i> = 69)	Mann-Whitney test
Age			
Median	76.47	76	<i>U</i> = 563.00, <i>p</i> = 0.79
Range	63–82	50–88	
Education			
Median	5	8	<i>U</i> = 472.00, <i>p</i> = 0.20
Range	3–14	3–18	
MMSE			
Median	28	28	<i>U</i> = 551.00, <i>p</i> = 0.69
Range	26–29	26–30	
<i>Intelligence</i>			
Raven			
Median	23	24	<i>U</i> = 546.50, <i>p</i> = 0.66
Range	9–36	6–36	
z-score	−1.19	−1.01	
<i>Memory</i>			
Rey Figure Drawing from Memory			
Median	7.5	7	<i>U</i> = 557.50, <i>p</i> = 0.75
Range	0–19	0–21	
<i>Visuo-spatial abilities</i>			
Trail Making A			
Median	68	68	<i>U</i> = 468.50, <i>p</i> = 0.20
Range	37–240	30–240	
Z-score	0.83	0.83	
Clock Drawing Test			
Median	6	9	<i>U</i> = 442.50, <i>p</i> = 0.11
Range	4–10	3–10	
Z-score	−2.45	0.27	
<i>Executive functions</i>			
Frontal Assessment Battery			
Median	12	13	<i>U</i> = 404.50, <i>p</i> = 0.047*
Range	8–18	6–18	
Z-score	−2.28	−1.72	

Note. Z-score equivalents are also included, calculated from normative data for Ravens Progressive Matrices (Basso et al., 1987), Trail Making A (Giovagnoli et al., 1996), the Clock Drawing test (Sunderland et al., 1989), and the Frontal Assessment Battery (Appollonio et al., 2004). Z-scores are not reported for the Rey Figure Drawing from Memory, as mean and standard deviation of the normal controls could not be found for this test.

**p* value uncorrected for multiple comparisons.

general structure to the copy (*n* = 12; 36.5%). These behaviors were also common in patients without CIB (57.5%) and did not specifically distinguish patients with CIB [$\chi^2(1) = 2.41$, n.s.].

To test for a special role of memory, our key comparison was between the frequency of CIB (near and overlap combined) in amnesic and non-amnesic MCI sub-groups. Numbers among the multi-domain sub-groups were sufficient to show clear sub-group differences, with CIB more than twice as common in the multidomain non-amnesic (*n* = 12; 41%) as in the multidomain amnesic sub-group (*n* = 19; 19%). A χ^2 test confirmed that this difference was significant [$\chi^2(1) = 5.86$; *p* < .02]. Few cases of CIB were found among the single-domain MCI sub-groups: none among the 12 single-domain non-amnesic sub-groups, and 2 among the single-domain amnesic sub-group.

Finally, to further explore the cognitive predictors of CIB, we studied the sub-sample of 86 patients who had completed the same cognitive assessment of memory, visuo-spatial and executive functions. CIB (near and overlap considered together) was found in 17 (20%) people among this sub-sample, being absent in the other 69 (80%). CIB was associated with good accuracy of the copy in 40% (*n* = 7) of the cases and with poor accuracy in 60% (*n* = 10) of the cases. An opposite pattern was observed in patients without CIB, whereby the copy was accurate in most of the cases (*n* = 45; 65%), while 24 patients (35%) presented constructional problems. However, this association between CIB and poor accuracy in the current sample did not reach significance [$\chi^2(1) = 3.29$; *p* = .07]. As shown in Table 2, those with CIB did not differ in age, education or MMSE from those without CIB, nor did they differ in memory performance or general intelligence.

The comparison between groups for visuospatial performance approached but did not reach statistical significance ($p = 0.20$ and $p = 0.11$), suggesting that their contribution was to some extent more important than other factors, such as memory or general intelligence. Overall, the FAB was the only task that significantly distinguished participants with and without CIB. Numerically, this effect was slight (one-point difference), but it was nonetheless reliable.

DISCUSSION

The present study shows for the first time that CIB, often studied in dementia, can also be observed in people with MCI. Ambron, McIntosh, et al. (2009) estimated the frequency of CIB to be 25% in a sample of 797 patients with AD copying simple geometric forms, and found that the frequency of CIB increases with the severity of the cognitive decline (see also Gainotti, 1972). In this context, the observed frequency of 21% in the present MCI sample (and 41% in the multidomain non-amnesic sub-group) may seem surprisingly high. However, the observed frequency of CIB in the MCI population is likely to have been biased considerably upward by the use of the Rey Figure, the most complex copying stimulus in common clinical use. It is indeed well established that more complex copying tasks are more likely to elicit CIB (e.g., Ambron, McIntosh, et al., 2009; Ambron, Della Sala, & McIntosh, 2009). It should also be noted that the clear majority (82%) of CIB manifestations in MCI were of the mild, "near" type, in which the copy is drawn close to the model, with only 18% of cases actually overlapping the model. Ambron, McIntosh, et al. (2009) found a more prominent representation of overlap type CIB (40% overlap, 60% near) in patients with AD, even with their simpler copying task.

The complexity of the Rey Figure also makes it sensitive to subtle constructional problems, and some constructional abnormalities were found in almost half (46%) of the MCI sample. Nonetheless, there was no significant association between these constructional abnormalities and CIB itself, reinforcing the idea that CIB is not a canonical manifestation of constructional apraxia (cf., Critchley, 1953). Rather, it may be a sign with distinct cognitive underpinnings, but which happens to be elicited often by constructional tasks (Ambron, McIntosh, et al., 2009; Ambron, Della Sala, et al., 2009; McIntosh et al., 2008).

The cognitive underpinnings of CIB were explored in MCI in the present study. First, to test the idea that CIB reflects an adaptive strategy to compensate for memory deficits (Lee et al., 2004), CIB frequency was compared between multidomain amnesic and non-amnesic MCI sub-groups. CIB was twice as common in the non-amnesic sub-group, in direct contradiction to a memory-based account. This main finding was strongly bolstered by the observation that patients with and without CIB did not differ on an explicit assessment of visuo-spatial memory, the Rey Figure Drawing from Memory. This could arguably be considered an ideal test for the idea that CIB reflects an inability to hold a representation of the model in mind, since retention of the

model is the key ability targeted. The lack of difference between CIB and non-CIB sub-groups on this task is strong evidence against memory-based compensation accounts of CIB (Lee et al., 2004).

Our comparison of CIB and non-CIB sub-groups, who were matched on major demographic and clinical variables, found that the only task discriminating between them was the FAB. The FAB is a well established assessment of executive functioning (Dubois et al., 2000; Kume et al., 2011), often applied to patients with dementia (Kugo et al., 2007; Lipton et al., 2005). Impairments of executive functions have been proposed to be responsible for the release of CIB within the framework of the attraction account (Kwon et al., 2002; McIntosh et al., 2008). The general idea is that CIB is the expression of a default sensorimotor organization in which the person tends to make manual responses towards the current focus of attention (i.e., the model during copying tasks). Executive control mechanisms normally inhibit this default tendency, allowing for actions to be decoupled from the attentional focus, but this inhibition can break down under conditions of reduced executive resources. The present findings are consistent with this hypothesis, and convergent with similar patterns of association in patients with AD (Ambron, McIntosh, et al., 2009), and in pre-school children displaying CIB during normal development (Ambron, McIntosh, & Della Sala, 2010). In the present study, the use of the Complex Rey Figure to assess CIB may have further emphasized the role of executive functions, as problems in planning might have caused some people to allow insufficient space for their copy, with the copy coming close to the model as a result.

It has further been proposed (McIntosh et al., 2008) that visuospatial factors may contribute additionally to the appearance of this default tendency, increasing the subjective difficulty of the task. This hypothesis could account for the high frequency of CIB in multi-domain non-amnesic MCI, whereby visuospatial functions were often compromised. On the other hand, the phenomenon was absent in single domain non-amnesic MCI. However, FAB performance, which proved to be predictive of CIB, was within normal limits in all but two of these patients. A dysexecutive basis for the release of CIB suggests a possible association of the phenomenon with other manifestations of dysexecutive impairment involving voluntary movements, such as the repetition of voluntary initiated movements (i.e., perseverations, Luria, 1966), or automatic grasp (magnetic apraxia) (Denny-Brown, 1958) or the compulsive use of visually or tactically presented objects (utilization behavior; Boccardi, Della Sala, Motto, & Spinnler, 2002; Lhermitte, 1983). To date, associations between these phenomena have been noted in passing by several studies but never systematically investigated. CIB has been associated with perseverations (Muncie, 1938; Wolfe et al., 1994), utilization behavior (Conson et al., 2009), and grasping reflex (De Ajuriaguerra et al., 1960; Kwon et al., 2002), in particular in patients suffering from specific frontal lobe dysfunctions (Conson et al., 2009; Kwon et al., 2002). On the other hand, this relation has not been supported in a study with patients with AD; Serra et al. (2010) found the same frequency of primitive reflexes in patients with and without CIB. A possible

explanation is that CIB may have a different nature in patients with AD and in patients with frontal lobe damage (Ambron, Allaria, et al., 2009). It has been proposed that visuospatial deficits may play a greater role in the appearance of CIB in AD, while the phenomenon may have a more primitive and automatic nature in patients with frontal lobe damage. Following this interpretation, CIB may be more likely to appear in conjunction with other primitive automatisms in patients with frontal lobe damage, as a direct expression of a dysexecutive impairment, than in patients with AD.

Reduced executive resources may thus be the principal determinant of CIB, but it should be emphasized that this conclusion applies especially to the relatively mild near-type CIB, most prevalent in the present MCI population. A similar study of a large AD sample (Ambron, McIntosh, et al., 2009) supported the association of near-type CIB with attentional function (measured by Digit Cancellation performance), but also found additional involvement of visuo-spatial impairments in the more severe overlap form of CIB. A further study (Serra et al., 2010), which looked at the predictors of overlap-type CIB *only*, in patients with AD, found an association with poor performance on visuo-spatial tests, but not with executive dysfunction. These studies, like the present one, were based on the analyses of pre-existing clinical records. The interpretation of such archival studies is limited by the fact that the cognitive assessments were not precisely targeted at the cognitive domains of interest, but were mapped onto those categories *post hoc*; and comparison between such studies is complicated by the different measures available in different archives. The lack of association between overlap-type CIB and executive resources suggested by Serra et al. (2010) was based on a non-significant difference between patients with and without CIB on a modified card sorting test; but it is possible that a wider-ranging assessment of executive functions, such as the FAB (used in this study), might have resulted in a stronger association.

A further limitation of our study is that the scoring procedure used to classify CIB was relatively arbitrary and may not have been sensitive enough to detect all the possible degree of CIB. A more quantitative measure of the phenomenon may possibly have provided a more sensitive measure of the phenomenon, detecting more subtle changes in the misplacement of the copy and being suitable for parametric analysis. On the other hand, the present assessment of CIB is consistent with several recent studies exploring CIB and provides reassurance that the observed behavior in patients with MCI is the same phenomenon classified as CIB in children (Ambron et al., 2010) and patients with dementia (Ambron, Allaria, et al., 2009; Ambron, McIntosh, et al., 2009). Moreover, information regarding the specific order in which the different elements were reproduced was not available. A detailed flow chart (Kaplan, 1998) would have increased and enriched the present classification of CIB, establishing whether a tendency to draw toward the model was characterized by a progressive or a more instant approach to the model. These different forms of migration toward the model have been noted in a previous study (McIntosh et al., 2008), but it is still unclear whether they represent different degrees or *qualities* of CIB.

The conclusions from archival studies ultimately need to be tested in more precisely-targeted prospective studies. However, a consistent picture is emerging from the recent analyses of CIB. Visuo-spatial impairments may be necessary for extreme manifestations of CIB in figure copying, which include scribbling over the top of the model, but the emergence of more subtle misplacement of the copy toward the model's space (near-type CIB) is primarily associated with reduced executive resources. The evidence from MCI supports this view. Moreover, the contrast between amnesic and non-amnesic sub-groups refutes the idea that CIB is associated with memory deficits (Lee et al., 2004).

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